FILE 'HOME' ENTERED AT 16:05:14 ON 25 AUG 2008

=> fil .bec

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

0.21 SESSION 0.21 0.21

FULL ESTIMATED COST

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS, ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 16:05:34 ON 25 AUG 2008 ALL COPPRIGHTS AND RESTRICTIONS APPLY. SEE HELP USAGETEEMS FOR DETAILS.

11 FILES IN THE FILE LIST

=> s casein kinase#

17975 CASEIN

312443 KINASE#

1 3761 CASEIN KINASE#

(CASEIN (W) KINASE#)

FILE 'SCISEARCH'

21279 CASEIN

352282 KINASE#

4167 CASEIN KINASE# (CASEIN(W)KINASE#)

FILE 'LIFESCI'

6138 "CASEIN"

103051 KINASE#

13 1586 CASEIN KINASE#

("CASEIN"(W)KINASE#)

FILE 'BIOTECHDS'

3162 CASEIN

12269 KINASE#

149 CASEIN KINASE# (CASEIN(W)KINASE#)

FILE 'BIOSIS'

L4

L5

L6

L8

37078 CASEIN 367328 KINASE#

3963 CASEIN KINASE#

(CASEIN(W)KINASE#)

FILE 'EMBASE'

15421 "CASEIN"

288673 KINASE# 3458 CASEIN KINASE#

("CASEIN" (W) KINASE#)

FILE 'HCAPLUS'

64026 CASEIN 337961 KINASE#

L7 4242 CASEIN KINASE#

(CASEIN(W)KINASE#)

FILE 'NTIS'

246 CASEIN

2118 KINASE#

7 CASEIN KINASE#

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(CASEIN(W)KINASE#)
FILE 'ESBIOBASE'
          7068 CASEIN
        157988 KINASE#
          1750 CASEIN KINASE#
L9
                 (CASEIN(W)KINASE#)
FILE 'BIOTECHNO'
          5488 CASEIN
         92256 KINASE#
L10
          1856 CASEIN KINASE#
                 (CASEIN(W)KINASE#)
FILE 'WPIDS'
         11050 CASEIN
         18683 KINASE#
           228 CASEIN KINASE#
                 (CASEIN(W)KINASE#)
TOTAL FOR ALL FILES
         25167 CASEIN KINASE#
=> s 112(10a)(sleep or circadian)
FILE 'MEDLINE'
         87589 SLEEP
         55873 CIRCADIAN
L13
            35 L1 (10A) (SLEEP OR CIRCADIAN)
FILE 'SCISEARCH'
         68569 SLEEP
         31939 CIRCADIAN
            33 L2 (10A) (SLEEP OR CIRCADIAN)
L14
FILE 'LIFESCI'
          7967 SLEEP
          9371 CIRCADIAN
L15
            23 L3 (10A) (SLEEP OR CIRCADIAN)
FILE 'BIOTECHDS'
           341 SLEEP
           171 CIRCADIAN
L16
             4 L4 (10A) (SLEEP OR CIRCADIAN)
FILE 'BIOSIS'
         75337 SLEEP
         40933 CIRCADIAN
L17
            44 L5 (10A) (SLEEP OR CIRCADIAN)
FILE 'EMBASE'
         79746 SLEEP
         39174 CIRCADIAN
L18
            29 L6 (10A) (SLEEP OR CIRCADIAN)
FILE 'HCAPLUS'
         24333 SLEEP
         24155 CIRCADIAN
1.19
            80 L7 (10A) (SLEEP OR CIRCADIAN)
FILE 'NTIS'
          2233 SLEEP
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933 CIRCADIAN

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0 L8 (10A) (SLEEP OR CIRCADIAN)
FILE 'ESBIOBASE'
         15346 SLEEP
         11181 CIRCADIAN
            28 L9 (10A) (SLEEP OR CIRCADIAN)
FILE 'BIOTECHNO'
          1338 SLEEP
          3773 CIRCADIAN
             7 L10(10A)(SLEEP OR CIRCADIAN)
FILE 'WPIDS'
         17799 SLEEP
           957 CIRCADIAN
1.23
             5 L11(10A) (SLEEP OR CIRCADIAN)
TOTAL FOR ALL FILES
           288 L12(10A) (SLEEP OR CIRCADIAN)
L24
=> s 112(10a) (muta? or variant# or allel? or polymorph?)
FILE 'MEDLINE'
        605690 MUTA?
        136049 VARIANT#
        135100 ALLEL?
        193129 POLYMORPH?
L25
           123 L1 (10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'SCISEARCH'
        597707 MUTA?
        156416 VARIANT#
        130911 ALLEL?
        233277 POLYMORPH?
           126 L2 (10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
L26
FILE 'LIFESCI'
        277175 MUTA?
         49074 VARIANT#
         65933 ALLEL?
         82555 POLYMORPH?
L27
           104 L3 (10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'BIOTECHDS'
         52383 MUTA?
         18614 VARIANT#
          9880 ALLEL?
         11873 POLYMORPH?
L28
            10 L4 (10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'BIOSIS'
        666734 MUTA?
        143237 VARIANT#
        159022 ALLEL?
        238789 POLYMORPH?
L29
           143 L5 (10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'EMBASE'
        512838 MUTA?
        119238 VARIANT#
        110681 ALLEL?
        168682 POLYMORPH?
L30
           111 L6 (10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
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```
FILE 'HCAPLUS'
        619116 MUTA?
        136680 VARIANT#
        133012 ALLEL?
        238659 POLYMORPH?
           198 L7 (10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'NTIS'
         10861 MUTA?
          5024 VARIANT#
           733 ALLEL?
          1792 POLYMORPH?
L32
             1 L8 (10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'ESBIOBASE'
        322887 MUTA?
         61245 VARIANT#
         75118 ALLEL?
         90873 POLYMORPH?
L33
           121 L9 (10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'BIOTECHNO'
        242571 MUTA?
         41198 VARIANT#
         55235 ALLEL?
         71286 POLYMORPH?
L34
           104 L10(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'WPIDS'
         39166 MUTA?
         36031 VARIANT#
          9945 ALLEL?
         12273 POLYMORPH?
1.35
             7 L11(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
TOTAL FOR ALL FILES
L36
          1048 L12(10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
=> s 136 and delta
FILE 'MEDLINE'
         87214 DELTA
L37
             8 L25 AND DELTA
FILE 'SCISEARCH'
        263384 DELTA
1.38
           12 L26 AND DELTA
FILE 'LIFESCI'
         47818 DELTA
L39
            13 L27 AND DELTA
FILE 'BIOTECHDS'
          4729 DELTA
             2 L28 AND DELTA
L40
FILE 'BIOSIS'
        128899 DELTA
1.41
            18 L29 AND DELTA
FILE 'EMBASE'
```

111663 DELTA

L45

FILE 'HCAPLUS'

508168 DELTA

35 L31 AND DELTA L43

FILE 'NTIS'

16164 DELTA

0 L32 AND DELTA

FILE 'ESBIOBASE'

66261 DELTA

14 L33 AND DELTA

FILE 'BIOTECHNO'

31359 DELTA

L46 8 L34 AND DELTA

FILE 'WPIDS'

37292 DELTA 0 L35 AND DELTA

TOTAL FOR ALL FILES

126 L36 AND DELTA L48

=> s csnk1d FILE 'MEDLINE'

3 CSNK1D

FILE 'SCISEARCH'

L50 2 CSNK1D

FILE 'LIFESCI'

L51 2 CSNK1D

FILE 'BIOTECHDS'

5 CSNK1D L52

FILE 'BIOSIS' L53

2 CSNK1D

FILE 'EMBASE'

2 CSNK1D

FILE 'HCAPLUS' L55 27 CSNK1D

FILE 'NTIS'

L56 0 CSNK1D

FILE 'ESBIOBASE'

L57 1 CSNK1D

FILE 'BIOTECHNO'

L58 1 CSNK1D

FILE 'WPIDS' L59 5 CSNK1D

TOTAL FOR ALL FILES L60 50 CSNK1D

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=> s 160(10a) (muta? or variant# or allel? or polymorph?)
FILE 'MEDLINE'
        605690 MUTA?
        136049 VARIANT#
        135100 ALLEL?
        193129 POLYMORPH?
             0 L49(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
1.61
FILE 'SCISEARCH'
        597707 MUTA?
        156416 VARIANT#
        130911 ALLEL?
        233277 POLYMORPH?
L62
             0 L50(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'LIFESCI'
        277175 MUTA?
         49074 VARIANT#
         65933 ALLEL?
         82555 POLYMORPH?
L63
             0 L51(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'BIOTECHDS'
         52383 MUTA?
         18614 VARIANT#
          9880 ALLEL?
         11873 POLYMORPH?
             0 L52(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
L64
FILE 'BIOSIS'
        666734 MUTA?
        143237 VARIANT#
        159022 ALLEL?
        238789 POLYMORPH?
             0 L53(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
L65
FILE 'EMBASE'
        512838 MUTA?
        119238 VARIANT#
        110681 ALLEL?
        168682 POLYMORPH?
L66
             0 L54(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'HCAPLUS'
        619116 MUTA?
        136680 VARIANT#
        133012 ALLEL?
        238659 POLYMORPH?
L67
             0 L55(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'NTIS'
         10861 MUTA?
          5024 VARIANT#
           733 ALLEL?
          1792 POLYMORPH?
L68
             0 L56(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'ESBIOBASE'
        322887 MUTA?
         61245 VARIANT#
         75118 ALLEL?
         90873 POLYMORPH?
```

T.82

```
FILE 'BIOTECHNO'
        242571 MUTA?
         41198 VARIANT#
         55235 ALLEL?
         71286 POLYMORPH?
L70
             0 L58(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
FILE 'WPIDS'
         39166 MUTA?
         36031 VARIANT#
          9945 ALLEL?
         12273 POLYMORPH?
             0 L59(10A)(MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
TOTAL FOR ALL FILES
L72
             0 L60(10A) (MUTA? OR VARIANT# OR ALLEL? OR POLYMORPH?)
=> s (148 or 124) not 2004-2008/py
FILE 'MEDLINE'
       3041907 2004-2008/PY
                 (20040000-20089999/PY)
L73
            21 (L37 OR L13) NOT 2004-2008/PY
FILE 'SCISEARCH'
       5727950 2004-2008/PY
                 (20040000-20089999/PY)
L74
            19 (L38 OR L14) NOT 2004-2008/PY
FILE 'LIFESCI'
        691170 2004-2008/PY
            19 (L39 OR L15) NOT 2004-2008/PY
L75
FILE 'BIOTECHDS'
        115051 2004-2008/PY
L76
            1 (L40 OR L16) NOT 2004-2008/PY
FILE 'BIOSIS'
       2596483 2004-2008/PY
           28 (L41 OR L17) NOT 2004-2008/PY
FILE 'EMBASE'
       2633738 2004-2008/PY
           22 (L42 OR L18) NOT 2004-2008/PY
L78
FILE 'HCAPLUS'
       6148426 2004-2008/PY
           44 (L43 OR L19) NOT 2004-2008/PY
L79
FILE 'NTIS'
         75409 2004-2008/PY
             0 (L44 OR L20) NOT 2004-2008/PY
L80
FILE 'ESBIOBASE'
       1505543 2004-2008/PY
1.81
            17 (L45 OR L21) NOT 2004-2008/PY
FILE 'BIOTECHNO'
           586 2004-2008/PY
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15 (L46 OR L22) NOT 2004-2008/PY

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FILE 'WPIDS'
       5246219 2004-2008/PY
1.83
             0 (L47 OR L23) NOT 2004-2008/PY
TOTAL FOR ALL FILES
L84
           186 (L48 OR L24) NOT 2004-2008/PY
=> dup rem 184
PROCESSING COMPLETED FOR L84
L85
            57 DUP REM L84 (129 DUPLICATES REMOVED)
=> d tot
L85 ANSWER 1 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
     Casein kinase i epsilon regulates transcription and period 2 stability
     within the mammalian circadian clock
     (2003) 105 pp. Avail.: UMI, Order No. DA3106752
SO
     From: Diss. Abstr. Int., B 2004, 64(9), 4197
ΑU
     Eide, Erik John
AN
     2004:622678 HCAPLUS
     142:88347
DN
L85 ANSWER 2 OF 57 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ΤI
     Screening methods for altering circadian rhythms and for human
     casein kinase I delta and/or epsilon phosphorylation of
     human clock proteins, period 1, -2 and -3.
     Official Gazette of the United States Patent and Trademark Office Patents,
     (Apr 29 2003) Vol. 1269, No. 5. http://www.uspto.gov/web/menu/patdata.html
     . e-file.
     ISSN: 0098-1133 (ISSN print).
AU
     Keesler, George A. [Inventor, Reprint Author]; Mondadori, Cesare
     [Inventor]; Yao, Zhengbin [Inventor]; Camacho, Fernando [Inventor]
     2003:248650 BIOSIS
AN
L85 ANSWER 3 OF 57
                      MEDLINE on STN
                                                        DUPLICATE 1
TT
     Phosphorylation of FREQUENCY protein by casein kinase
     II is necessary for the function of the Neurospora circadian
     clock.
so
     Molecular and cellular biology, (2003 Sep) Vol. 23, No. 17, pp. 6221-8.
     Journal code: 8109087. ISSN: 0270-7306.
AII
    Yang Yuhong; Cheng Ping; He Oivang; Wang Lixin; Liu Yi
AN
    2003381810
                   MEDLINE
L85 ANSWER 4 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
```

- TI Isolation of suppressor mutants of phosphatidylinositol 3-phosphate
- 5-kinase deficient cells in Schizosaccharomyces pombe
- SO Bioscience, Biotechnology, and Biochemistry (2003), 67(8), 1772-1779 CODEN: BBBIEJ; ISSN: 0916-8451
- AU Onishi, Masayuki; Nakamura, Yoko; Koga, Takako; Takegawa, Kaoru; Fukui, Yasuhisa
- AN 2003:721504 HCAPLUS
- DN 139:375942
- L85 ANSWER 5 OF 57 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
- TI Comparative analysis of avian BMAL1 and CLOCK protein sequences: A search for features associated with owl nocturnal behaviour.
- SO Comparative Biochemistry and Physiology Part B Biochemistry & Molecular Biology, (December 2003) Vol. 136B, No. 4, pp. 861-874. print. ISSN: 1096-4959 (ISSN print).
- AU Fidler, Andrew E. [Reprint Author]; Gwinner, Eberhard
- AN 2004:98668 BIOSIS

- L85 ANSWER 6 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
- TI Circadian rhythm and sleep disorders
- SO Igaku no Ayumi (2003), 204(11), 799-802 CODEN: IGAYAY; ISSN: 0039-2359
- AU Ebisawa, Takashi
- AN 2003:362521 HCAPLUS
- DN 139:177551
- L85 ANSWER 7 OF 57 MEDLINE on STN DUPLICATE 2
- TI CK1 and GSK3 in the Drosophila and mammalian circadian clock.
- SO Novartis Foundation symposium, (2003) Vol. 253, pp. 267-77; discussion 102-9, 277-84. Journal code: 9807767. ISSN: 1528-2511.
- AU Harms Emily; Young Michael W; Saez Lino
- AN 2004015503 MEDLINE
- L85 ANSWER 8 OF 57 MEDLINE on STN
- TI A role for CK2 in the Drosophila circadian oscillator.
- SO Nature neuroscience, (2003 Mar) Vol. 6, No. 3, pp. 251-7.
- Journal code: 9809671. ISSN: 1097-6256.
- AU Akten Bikem; Jauch Eike; Genova Ginka K; Kim Eun Young; Edery Isaac; Raabe Thomas; Jackson F Rob

- AN 2003089891 MEDLINE
- L85 ANSWER 9 OF 57 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
- TI A new role for an old kinase: CK2 and the circadian clock.
- SO Nature Neuroscience, (1 Mar 2003) Vol. 6, No. 3, pp. 208-210. Refs: 13
- ISSN: 1097-6256 CODEN: NANEFN AU Blau, Justin (correspondence)
- AN 2003099617 EMBASE
- L85 ANSWER 10 OF 57 LIFESCI COPYRIGHT 2008 CSA on STN DUPLICATE 4
- TI Mutant casein kinase I (Hrr25p/Kti14p)
- abrogates the G1 cell cycle arrest induced by Kluyveromyces lactis zymocin in budding yeast

  S0 Molecular Genetics and Genomics [Mol. Genet. Genomics], (20030500) vol.
- SO Molecular Genetics and Genomics [Mol. Genet. Genomics], (20030500) vol 269, no. 2, pp. 188-196. ISSN: 1617-4615.
- AU Mehlgarten, C.; Schaffrath, R.
- AN 2003:64326 LIFESCI
- L85 ANSWER 11 OF 57 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on SIN
  - TI Casein kinase i and circadian rhythms:
    - effects of manipulation of ckiepsilon activity on period.
- SO Society for Neuroscience Abstract Viewer and İtinerary Planner, (2003) Vol. 2003, pp. Abstract No. 284.3. http://sfn.scholarone.com. e-file. Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
- AU Camacho, F. [Reprint Author]; Hurst, W. J. [Reprint Author]; Vielhaber, E. [Reprint Author]; Harnish, S. [Reprint Author]; Roehr, J. [Reprint Author]; Author]; Friedman, E. [Reprint Author]; Menaker, M.; Khorkova, O. [Reprint Author]; Virshup, D.; Giovanni, A. [Reprint Author]
- AN 2004:196776 BIOSIS
- L85 ANSWER 12 OF 57 BIOTECHDS COPYRIGHT 2008 THOMSON REUTERS on STN
- TI Novel hPER2 gene or its mutant form, that participates in the human circadian biological clock, useful as marker for diagnosing familial advanced sleep phase syndrome in human subject;
  - recombinant protein production via plasmid expression in host cell use

in disease therapy

- AΠ PTACEK L; FU Y; JONES C; VIRSHUP D
- AΝ 2002-19973 BIOTECHDS
- PT WO 2002055667 18 Jul 2002
- L85 ANSWER 13 OF 57 MEDLINE on STN
- DUPLICATE 5
  - The circadian regulatory proteins BMAL1 and cryptochromes are substrates of casein kinase Iepsilon.
- SO The Journal of biological chemistry, (2002 May 10) Vol. 277, No. 19, pp. 17248-54. Electronic Publication: 2002-03-01. Journal code: 2985121R. ISSN: 0021-9258.
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- AN 2002253137 MEDLINE
- L85 ANSWER 14 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
- TT Oscillatory mechanism of mammalian circadian rhythm SO Tanpakushitsu Kakusan Koso (2002), 47(14), 1914-1923
- CODEN: TAKKAJ; ISSN: 0039-9450 Nagai, Katsuya; Isojima, Yasushi; Okumura, Nobuaki ΑU
- AN 2002:824521 HCAPLUS
- DN 137:335384
- L85 ANSWER 15 OF 57 MEDLINE on STN
- DUPLICATE 6 TI Control of intracellular dynamics of mammalian period proteins by casein
- kinase I epsilon (CKIepsilon) and CKIdelta in cultured cells.
- Molecular and cellular biology, (2002 Mar) Vol. 22, No. 6, pp. 1693-703. SO Journal code: 8109087. ISSN: 0270-7306.
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- L85 ANSWER 16 OF 57 MEDLINE on STN
- DUPLICATE 7

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- Genes & development, (2002 Apr 15) Vol. 16, No. 8, pp. 994-1006. SO
- Journal code: 8711660. ISSN: 0890-9369.
- AII Yang Yuhong; Cheng Ping; Liu Yi
- AN 2002222772 MEDLINE
- L85 ANSWER 17 OF 57 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
- TI Sequential multisite phosphorvlation by casein kinase I epsilon (CKIepsilon).
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- L85 ANSWER 18 OF 57 MEDLINE on STN
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- AN 2002728581 MEDITNE
- L85 ANSWER 19 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
- TI The Drosophila clock protein Timeless is a member of the Arm/HEAT family
- SO Current Biology (2002), 12(18), R610-R611

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- L85 ANSWER 20 OF 57 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
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- L85 ANSWER 21 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
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- Molecular Biology of the Cell (2002), 13(1), 362-381 SO
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- AN DN 136:229625
- L85 ANSWER 22 OF 57 MEDLINE on STN
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- SO BMC neuroscience, (2002 Dec 20) Vol. 3, pp. 20. Electronic Publication: 2002-12-20.
  - Journal code: 100966986. E-ISSN: 1471-2202.
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- DN 137:198824
- L85 ANSWER 24 OF 57 LIFESCI COPYRIGHT 2008 CSA on STN DUPLICATE 9
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- AN 2001:377953 SCISEARCH
- L85 ANSWER 27 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
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L85 ANSWER 6 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN

AB A review on candidate genes in human circadian rhythm sleep disorders.
The topics discussed are (1) association of polymorphisms of the period3 (Per3) gene, casein kinase lc gene and
melatonin la receptor gene with delayed sleep phase syndrome
(USPS) and non-24-h sleep-wake syndrome (N-24); and (3) polymorphisms of
the period2 (Per2) and clock genes in advanced sleep phase syndrome
(ASPS).

L85 ANSWER 7 OF 57 MEDLINE on STN

DUPLICATE 2

Two kinases, DOUBLETIME and SHAGGY, have been shown to play a role in the circadian clock. DOUBLETIME, the Drosophila orthologue of casein kinase 1, can phosphorylate PERIOD in the cytoplasm and in the nucleus. This phosphorylation destabilizes PERIOD in both locations and sets patterns of both cytoplasmic accumulation and nuclear turnover. Cytoplasmic phosphorylation postpones accumulation of PERIOD TIMELESS complexes. SHAGGY, the Drosophila orthologue of glycogen synthase kinase 3, phosphorylates TIMELESS and promotes nuclear translocation of PERIOD TIMELESS complexes. Thus, the opposing effects of these two kinases in the cytoplasm are crucial for establishing the approximately 24 h period of circadian rhythmicity in Drosophila. Casein Kinase 1 has been shown to be a component of the circadian clock in mammals. Recent studies are also pointing to a role for glycogen synthase kinase 3 in the mammalian clock.

- L85 ANSWER 10 OF 57 LIFESCI COPYRIGHT 2008 CSA on STN DUPLICATE 4
- Zymocin, a toxic protein complex produced by Kluyveromyces lactis, AB inhibits cell cycle progression in Saccharomyces cerevisiae. In studying its action, a resistant mutant (kti14-1) was found to express the tot-phenotype typical of tot Delta cells, toxin target (TOT) mutants that are impaired in RNA polymerase II Elongator function. Phenotypic analysis of a kti14-1 tot3 Delta double mutant revealed a functional link between KTI14 and TOT /Elongator. Unlike tot Delta cells, the kti14-1 mutant is sensitive to the drug methylmethane sulfonate (MMS), indicating that, besides being affected in TOT function, ktil4-1 cells are also compromised in DNA repair. Single-copy complementation identified HRR25, which codes for casein kinase I (CKI), as KTI14. Kinase-minus hrr25 mutations (K38A and T176I) conferred zymocin resistance, while deletion of the other yeast CKI genes (YCK1-3) had no effect. A mutation in KTI14 that truncates the P/O-rich C-terminus of Hrr25p also dissociates MMS sensitivity from zymocin resistance; this mutant is resistant to the toxin, but shows normal sensitivity to MMS. Thus, although kinase-minus mutations are sufficient to protect yeast cells from zymocin, toxicity is also dependent on the integrity of the C-terminal region of Hrr25p, which has been implicated in determining the substrate specificity or localization of Hrr25p.
- L85 ANSWER 11 OF 57 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
- AB Post-translational modification of molecular clock components has been implicated as a critical regulator of circadian rhythms. Phosphorylation of PERIOD (PER) by casein kinase I epsilon (CKIepsilon) appears to be a key component of the molecular clock that drives circadian rhythms in the central pacemaker and periphery. Drosophila with mutations in the

dCKIepsilon gene, double-time (dbt), demonstrated lengthening or shortening of period. The tau hamster contains a mutation in CKIepsilon that renders the enzyme less effective in phosphorylating PER, and the mutation on the CKIepsilon phosphorylation site in hPer2 identified in a family with advanced sleep phase syndrome (FASPS) appear to relate decreased phosphorylation by CKIepsilon to a shortening of period. In these studies we assessed the effects of CKIepsilon modulation on PER phosphorylation and how this relates to the circadian rhythm of the molecular clock. Over expression of kinase dead CKIepsilon (K38A) in Rat-1 fibroblast induced a longer phase on Rev-erba, a circadian controlled gene. In contrast, over expression of CKIepsilon induced a shortened phase on Rev-erba. Using the commercially available CKIepsilon inhibitors Icos-261 and CK1-7 we demonstrate a dose dependent decrease in phosphorylated PER (1 and 2) in transfected cells. Furthermore, using a Rat-1 Perl-luc circadian cell model (see Hurst et al. Neuroscience 2003) we show that both Icos-261 and CK1-7 induce a significant, dose dependent increase in period with an estimated 1h lengthening occurring at 1-10 uM. Our findings on the circadian effects of modulating CKIepsilon activity contrasts the phenotype observed in the tau hamster and FASPS, but further illuminate the critical role of CKIepsilon in the regulation of the circadian clock.

- L85 ANSWER 14 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
- AB A review on the mammalian oscillating mechanism and proteins involved therein, discussing characteristics of circadian rhythm, circadian oscillation by pos.-neg. feedback loop, identification and functional anal. of oscillating proteins in the suprachiasmatic nucleus (SCN), such as SCOP (SCN circadian oscillatory protein), casein kinase ls (CKIs), PIPS (Perl interacting protein of the SCN), and BIT/SHIPS1.
- L85 ANSWER 15 OF 57 MEDLINE on STN DUPLICATE 6
- Recent studies have shown that casein kinase I epsilon AB (CKIepsilon) is an essential regulator of the mammalian circadian clock. However, the detailed mechanisms by which CKIepsilon regulates each component of the circadian negative-feedback loop have not been fully defined. We show here that mPer proteins, negative limbs of the autoregulatory loop, are specific substrates for CKIepsilon and CKIdelta. The CKI phosphorylation of mPer1 and mPer3 proteins results in their rapid degradation, which is dependent on the ubiquitin-proteasome pathway. Moreover, CKIepsilon and CKIdelta are able to induce nuclear translocation of mPer3, which requires its nuclear localization signal. The mutation in potential phosphorylation sites on mPer3 decreased the extent of both nuclear translocation and degradation of mPer3 that are stimulated by CKIepsilon. CKIepsilon and CKIdelta affected the inhibitory effect of mPer proteins on the transcriptional activity of BMAL1-CLOCK, but the inhibitory effect of mCrv proteins on the activity of BMAL1-CLOCK was unaffected. These results suggest that CKIepsilon and CKIdelta regulate the mammalian circadian autoregulatory loop by controlling both protein turnover and subcellular localization of mPer proteins.
- L85 ANSWER 27 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
- AB We have examined posttranslational regulation of clock proteins in mouse liver in vivo. The mouse PERIOD proteins (mpERI and mpERE), CLOCK, and BMAL1 undergo robust circadian changes in phosphorylation. These proteins, the cryptochromes (mcRY1 and mcRY2), and casein kinase I epsilon (CKIE) form multimeric complexes that are bound to DNA during neg. transcriptional feedback. CLOCK:BMAL1 heterodimers remain bound to DNA over the circadian cycle. The temporal increase in mPER abundance controls the neg. feedback interactions. Anal. of clock proteins in mCRY-deficient mice shows that the mCRYs are necessary for stabilizing phosphorylated mPERE2 and for the nuclear accumulation of mPER1, mPER2, and

CKIs. We also provide in vivo evidence that casein kinase I delta is a second clock relevant kinase.

- L85 ANSWER 29 OF 57 MEDLINE on STN DUPLICATE 12
- AB Multiple components of the circadian central clock are phosphoproteins, and it has become increasingly clear that posttranslational modification is an important regulator of circadian rhythm in diverse organisms, from dinoflagellates to humans. Genetic studies in Drosophila have identified double-time (dbt), a serine/threonine protein kinase that is highly homologous to human casein kinase I epsilon (CKIepsilon), as the first kinase linked to behavioral rhythms. Identification of a missense mutation in CKIepsilon as the tau mutation in the Syrian hamster places CKIepsilon within the core clock machinery in mammals. Most recently, identification of a phosphorylation site mutant of hPER2 in a family with an inherited circadian rhythm abnormality strongly suggests that PER2 is a physiologically relevant substrate of CKI. Phosphorylation may regulate multiple properties of clock proteins, including stability and intracellular localization.
- L85 ANSWER 30 OF 57 MEDLINE on STN
- DUPLICATE 13 Casein kinase Iepsilon (CKIepsilon), a central AB component of the circadian clock, interacts with and phosphorylates human period protein 1 (hPER1) [Keesler, G.A. et al. (2000) NeuroReport 5, 951-955]. A mutation in CKIepsilon causes a shortened circadian period in Syrian Golden hamster. We have now extended our previous studies to show that human casein kinase Idelta (hCKIdelta), the closest homologue to hCKIepsilon, associates with and phosphorylates hPER1 and causes protein instability. Furthermore, we observed that both hCKIdelta and hCKIepsilon phosphorylated and caused protein instability of human period 2 protein (hPER2). Immunohistochemical staining of rat brains demonstrates that CKIdelta protein is localized in the suprachiasmatic nuclei, the central location of the master clock. These results indicate that CKIdelta may play a role similar to CKIepsilon, suggesting that it may also be involved in regulating circadian rhythmicity by post-translation modification of mammalian clock proteins hPER1 and 2.
- L85 ANSWER 31 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
- A review with 52 refs. The casein kinase I (CKI) family of protein kinases is a group of highly related, ubiquitously expressed serine/threonine kinases found in all eukarvotic organisms from protozoa to man. Recent advances in diverse fields, including developmental biol. and chronobiol., have elucidated roles for CKI isoforms in regulating critical processes such as Wnt signaling, circadian rhythm, NF-AT4 nuclear import, and Alzheimer's disease progression.
- L85 ANSWER 33 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN Unavailable AB
- L85 ANSWER 47 OF 57 HCAPLUS COPYRIGHT 2008 ACS on STN
- Protein kinase mutant and wild-type genes encoding polypeptides AB of the class designated casein kinase I and useful in screening compns. which may affect DNA double-strand break repair activity are disclosed. Also disclosed are methods using the polynucleotides in cell-proliferative disorders. Specifically illustrating the invention are Saccharomyces cerevisiae DNAs including those encoding HRR25 and NUF1, Schizosaccharomyces pombe DNAs including those encoding Hhpl+ and Hhp2+, and human DNAs including those encoding CKIalHu, CHIa2Hu, CHIα3Hu, CHIγ1Hu, CHIγ2Hu, and CHI δ Hu.

Also provided are autonomously replicating recombinant constructions such as plasmid and viral DNA vectors incorporating such sequences and especially vectors wherein DNA encoding an HRR25-like casein kinase I protein is

linked to an endogenous or exogenous expression control DNA sequence. Monoclonal antibodies specific or HRR25-like proteins were secreted by hybridomas 75C10H, 80J9E, 94AlD, 94F4A, 94J1lc, and 128A.

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- SO PCT Int. Appl., 268 pp.
- CODEN: PIXXD2
- IN Tononi, Giulio; Cirelli, Chiara
- AN 2005:589224 HCAPLUS
- DN 143:92115

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TI New isolated casein kinase I delta nucleic and casein											
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